



European Code against Cancer 4th Edition: 12 ways to reduce your cancer risk[☆]



Joachim Schüz^{a,1,*}, Carolina Espina^{a,1}, Patricia Villain^{a,1}, Rolando Herrero^{a,1}, Maria E. Leon^{a,1}, Silvia Minozzi^{b,1}, Isabelle Romieu^{a,1}, Nereo Segnan^{b,1}, Jane Wardle^{c,1}, Martin Wiseman^{d,1}, Filippo Belardelli^{e,2}, Douglas Bettcher^{f,2}, Franco Cavalli^{g,2}, Gauden Galea^{h,2}, Gilbert Lenoir^{i,2}, Jose M. Martin-Moreno^{j,2}, Florian Alexandru Nicula^{k,2}, Jørgen H. Olsen^{l,2}, Julietta Patnick^{m,2}, Maja Primic-Zakelj^{n,2}, Pekka Puska^{o,2}, Flora E. van Leeuwen^{p,2}, Otmar Wiestler^{q,2}, Witold Zatonski^{r,2}; Working Groups of Scientific Experts³

^a International Agency for Research on Cancer (IARC), Lyon, France

^b CPO Piedmont, University Hospital "Città della Salute e della Scienza", Turin, Italy

^c University College London, London, UK

^d World Cancer Research Fund International, London, UK

^e Istituto Superiore di Sanità, Rome, Italy

^f World Health Organization, Geneva, Switzerland

^g Oncology Institute of Southern Switzerland, Bellinzona, Switzerland

^h World Health Organization Regional Office for Europe, Copenhagen, Denmark

ⁱ Institut Gustave Roussy, Villejuif, France

^j University of Valencia, Valencia, Spain

^k Oncology Institute "Prof. Dr I. Chiricuta", Cluj-Napoca, Romania

^l Danish Cancer Society Research Center, Copenhagen, Denmark

^m Public Health England, Sheffield, UK

ⁿ Institute of Oncology, Ljubljana, Slovenia

^o National Institute for Health and Welfare, Helsinki, Finland

^p Netherlands Cancer Institute, Amsterdam, The Netherlands

^q German Cancer Research Center (DKFZ), Heidelberg, Germany

^r Maria Skłodowska-Curie Cancer Center and Institute of Oncology, Warsaw, Poland

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ABSTRACT

This overview describes the principles of the 4th edition of the European Code against Cancer and provides an introduction to the 12 recommendations to reduce cancer risk. Among the 504.6 million inhabitants of the member states of the European Union (EU28), there are annually 2.64 million new cancer cases and 1.28 million deaths from cancer. It is estimated that this cancer burden could be reduced by up to one half if scientific knowledge on causes of cancer could be translated into successful prevention. The Code is a preventive tool aimed to reduce the cancer burden by informing people how to avoid or reduce carcinogenic exposures, adopt behaviours to reduce the cancer risk, or to participate in organised intervention programmes. The Code should also form a base to guide national health policies

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Abbreviations: DG SANTE, Directorate-General for Health and Food Safety; EC, European Commission; EU, European Union; HPV, human papilloma virus; HBV, hepatitis B virus; HIV, human immunodeficiency virus; HRT, hormone replacement therapy; IARC, International Agency for Research on Cancer; PICOS, Population, Intervention, Control, Outcome, Study design; UK, United Kingdom; UV, ultraviolet; UVR, ultraviolet radiation; WG, working group; WCRF/AICR, World Cancer Research Fund/American Institute of Cancer Research; WHO, World Health Organization.

* Corresponding author at: IARC European Code against Cancer Secretariat, 150 Cours Albert Thomas, 69372 Lyon Cedex 08, France. Tel.: +33 0 4 72 73 84 85.

E-mail address: secretariat-cancer-code-europe@iarc.fr (J. Schüz).

¹ Members of the Scientific Secretariat and/or Chairs of Expert Working Groups (as shown in Fig. 2).

² Members of the European Code against Cancer Scientific Committee.

³ (See Appendix).

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in cancer prevention. The 12 recommendations are: not smoking or using other tobacco products; avoiding second-hand smoke; being a healthy body weight; encouraging physical activity; having a healthy diet; limiting alcohol consumption, with not drinking alcohol being better for cancer prevention; avoiding too much exposure to ultraviolet radiation; avoiding cancer-causing agents at the workplace; reducing exposure to high levels of radon; encouraging breastfeeding; limiting the use of hormone replacement therapy; participating in organised vaccination programmes against hepatitis B for newborns and human papillomavirus for girls; and participating in organised screening programmes for bowel cancer, breast cancer, and cervical cancer.

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1. Introduction

Cancer is the second leading cause of death in Europe [1]. For the 28 member states of the EU (EU28) – which are Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom (UK) – with a total population of 504.6 million inhabitants in 2012, the estimated cancer burden for 2012 was approximately 1.43 million new cancer cases in men and 1.21 million new cancer cases in women, and 716,000 cancer deaths in men and 561,000 cancer deaths in women, all figures excluding non-melanoma skin cancer [2].

It has been estimated that up to half of the cancer burden is preventable [3,4]. Successful prevention requires a combination of individual preventive action (by avoiding or reducing harmful exposures) and group action (when exposure is eliminated or reduced by measures effective at the population level). For individuals to engage in successful prevention and reduction of their cancer risk, they need to be informed about evidence-based actions to reduce their risk of cancer. The European Code against Cancer is a set of recommendations providing such advice on prevention of cancer. Its 3rd edition, published in 2003 [5] (originally the Code was developed in 1987 and revised in 1994), lists seven recommendations on the adoption of healthier lifestyles to improve many aspects of general health and the prevention of many cancer deaths; four recommendations were listed as successful interventions (screening and vaccinations). With the dynamics of expanding knowledge intrinsic in science, the European Commission mandated the International Agency for Research on Cancer (IARC) based in Lyon (France) to revise the 3rd edition, taking into account the most up-to-date and best available scientific evidence on causation and prevention of cancer. Working Groups (WGs) were established accordingly to revise the existing recommendations or suggest additional recommendations where new scientific evidence had become available. A Scientific Committee of lead experts on cancer prevention in Europe was established to review the suggestions, and then to approve the final version.

Here, we present an overview of the principles of the European Code against Cancer update and the definition of the target population, the methods used by the WGs to update the evidence, and the principles of communication to ensure the recommendations are fully understood by the target audience, namely the European citizen. Most importantly, here we present the 4th edition of the European Code against Cancer.

2. Principles and methods

2.1. Principles

The European Code against Cancer 4th edition was built on the following four principles:

- 1) Sufficient scientific evidence that following the recommendation to avoid or reduce exposure to a harmful agent, or to adopt a healthy behaviour, or participate in screening or vaccination activities would reduce the individual's risk of developing cancer or dying from cancer.

All recommendations needed to be scientifically justified, following procedures outlined below. Importantly, the Code aims at causes of cancer or interventions shown to reduce the risk of developing or dying from cancer; hence, for the individual there is a scientifically established benefit, albeit obviously acknowledging the impossibility of totally avoiding cancer. Avoiding exposures of possible carcinogenicity where there is scientific uncertainty is not part of the recommendations.

- 2) The recommendations are suitable for a broad target population.

It was ensured that recommendations be applicable to a broad target audience. The intention was not to neglect or downplay risks, particularly affecting vulnerable groups (e.g., smaller high-risk groups), but it was felt that they needed preventive efforts more focused on their particular requirements. For such situations, however, the Code attempts to raise awareness in the general population by providing information (see below).

- 3) The recommendation is something individuals can do to reduce their cancer risk.

As outlined above, successful prevention is a combination of individual actions and policies and community actions. A principle in the recommendations of the 4th edition of the European Code against Cancer was to focus on risks modifiable by the individual. The intention was not to downplay the responsibility of health decision-makers, but to provide a tool for people responding to the question “what can I do to reduce my cancer risk”.

- 4) The recommendation can be clearly and succinctly communicated to the general population.

Another principle was to avoid recommendations that would give confusing or mixed messages to people. This is particularly the case when an individual risk–benefit analysis is needed to assess whether the exposure carries a benefit that may outweigh the potential risk. An example is exposure to medical radiation. X-rays are carcinogenic to humans; however, refusing an imaging examination may have fatal consequences [6,7]. Also some pharmaceuticals fall into this category [7]. Therefore, each recommendation was phrased in a way that it: (i) can be understood by the general population, (ii) is memorable and/or recognisable, (iii) creates a sense that cancer can be prevented, (iv) enhances motivation to change, and (v) can be used across Europe as a basis for public education.

2.2. Presentation

A conceptual structure for the presentation of the European Code against Cancer was developed and comprises three levels of information (Fig. 1). The work was performed under the work-flow and decision-making structure shown in Fig. 2. The six topic-related Working Groups (WGs) dealt with smoking and other forms of tobacco use (WG Tobacco); with diet, physical activity, body weight and alcohol consumption (WG Nutrition); with environmental and occupational exposures and pharmaceuticals (WG Environment); with radiation (WG Radiation); with infections and vaccinations (WG Infections); and with cancer screening (WG Screening). Additional WGs were established for the literature search (Literature Group) and for communication (WG Communication, see below).

Level I is the Code itself, which includes the 12 recommendations following the principles explained in the previous section. The recommendations were proposed by expert WGs according to the methodology described in the next section. The proposals were checked and sometimes revised by the WG Communication for clarity of the message given to a general population audience. There were sometimes several iterations between the experts on the topic and the experts on communication, to achieve a consensus to be presented to the Scientific Committee. The Scientific Committee – consisting of 14 senior cancer experts from leading European cancer research and prevention institutions – were provided with the list of recommendations; during two meetings in September 2013 and February 2014 these were discussed, and the recommendations were finally approved. In case of lack of consensus on any recommendation, a formal voting process had been defined for the Scientific Committee, with the final decision based on a simple majority vote. In practice, there was always consensus on accepting the scientific basis provided by the WGs to justify the recommendations, but voting was applied in some instances when two versions of phrasings were available or whether a statement should be part of the recommendation or provided on level II (see below). All Scientific Committee members approved the final list of recommendations in its totality.

Level II was newly introduced in the 4th edition. Like level I, its aim was to inform the general public. Level II was developed in question-and-answer-format, explaining and providing additional information on the recommendations as well as cancer prevention topics not covered in level I: for instance on carcinogenic agents not being part of any of the recommendations of the Code for the reason of not fulfilling all the principles outlined in the previous section. Level II was developed by the expert WGs – both the questions and their answers. This was then reviewed by the Working Group on Communication and by the Scientific Committee. However, the final decisions regarding level II on what and how to present remained the responsibility of the experts on the topic, i.e. the respective WG. Typical questions shown on level II are further information on exposure, messages for special target groups, and information on practical preventive actions on how to best follow the recommendation.

Level III is the scientific justification of the recommendations, including the justification of each recommendation of level I and the scientific statements made in level II. Those are the peer-reviewed publications of the current special issue and are written in scientific language.

2.3. Methodology

A detailed description of the methodology is provided elsewhere [8]. In brief, for a risk factor or an intervention to be considered as recommendation it had to comply with the principles outlined under “Principles”.

For confirming evidence of carcinogenicity to humans, it was decided to use the IARC Monograph series on the Evaluation of Carcinogenic Risks to Humans [9,10] (mainly for physical, chemical or biological factors) and the Expert Reports and Continuous Update Project of the World Cancer Research Fund/American Institute of Cancer Research (WCRF/AICR) (mainly for topics related to food, nutrition, physical activity and the prevention of cancer) [11,12]. If the topic was not recently evaluated, or if the WG felt that more recent scientific literature may alter this evaluation, a systematic literature review was invoked. For this purpose, a Literature Group was established comprising scientific

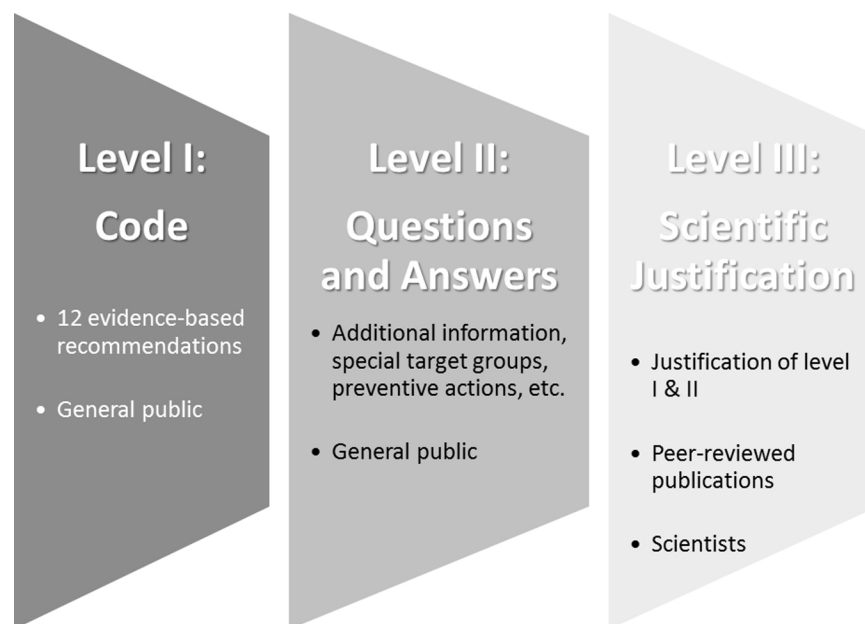


Fig. 1. Conceptual structure of the 4th edition of the European Code against Cancer; level I: recommendations on 12 ways to reduce your cancer risk (to the general public); level II: questions and answers related to the 12 ways to reduce your cancer risk, including clarifications, messages to specific target groups, and interventions to reduce exposure, as well as to cancer prevention in general (to the general public); level III: scientific justification of the recommendations (to experts by means of peer-reviewed publications).

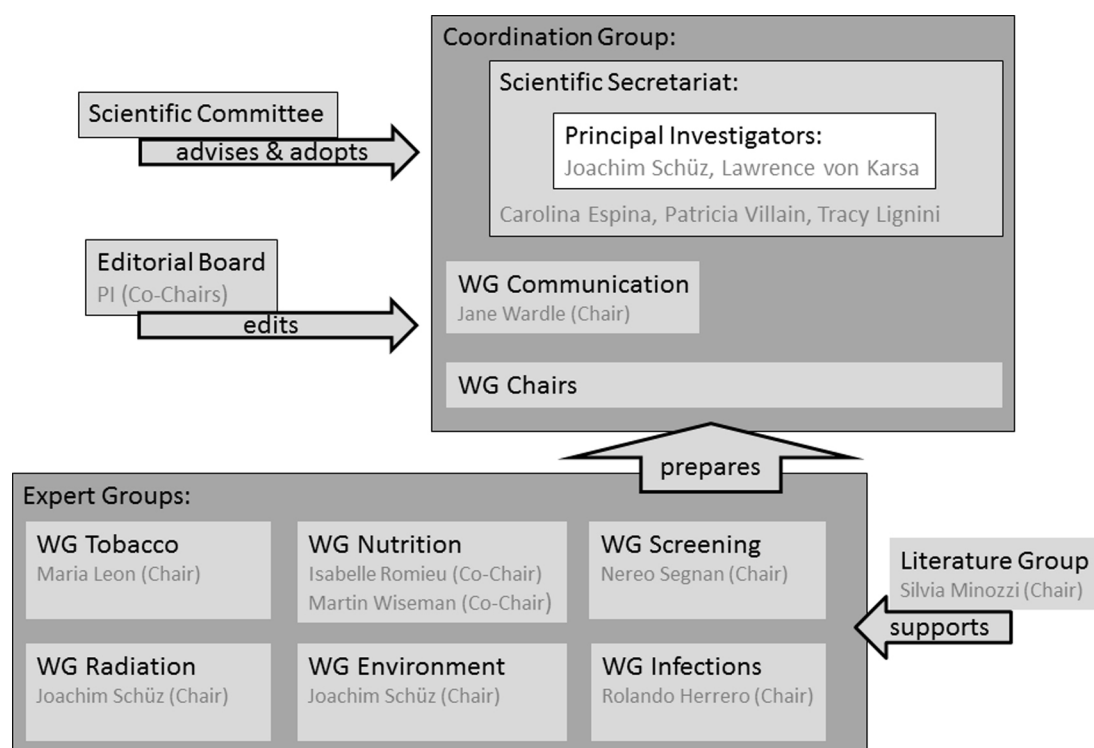


Fig. 2. Work flow and decision-making structure for the 4th edition of the European Code against Cancer; WG, Working Group; PI, principal investigator.

experts experienced in searching and evaluating scientific literature. More details are given elsewhere [8].

For interventions, it was decided to use the IARC Handbooks of Cancer Prevention, the World Health Organisation (WHO) position papers, and the European Guidelines for Quality Assurance in Cancer Screening [8], complemented by comprehensive systematic reviews performed by the Literature Group following PICOS methodology [13–15]. This was applied to the topics of smoking cessation, vaccinations, and for screening. More details can be found elsewhere [16–18].

2.4. Dissemination

In order to disseminate the messages and scientific basis of the 4th edition of the European Code against Cancer, the Code was launched on the 14th October 2014 by the IARC in a joint press conference with the participation of the Directorate-General for Health and Food Safety (DG SANTE) from the European Commission (EC) and IARC representatives. The European Code against Cancer is available on the EC and IARC websites [19,20]. Questions and answers that provide additional information about the recommendations and the different types of cancer they help to prevent are also published on the IARC website [20]. The scientific justifications for the Code are published in this issue and will be made available to the general public on the IARC website as well. In addition to English, the Code and the questions and answers will be available in 22 other EU official languages.

3. Results: 12 recommendations

The 4th edition of the European Code against Cancer describes “12 ways to reduce your cancer risk” (Box 1). The recommendations were developed to enable and encourage individuals to modify their own cancer risk, to address a relevant cancer burden, and to be understandable by the general population. They covered

the following areas: tobacco smoking and use of other forms of tobacco; second-hand smoke; healthy body weight; physical activity; healthy diet; alcohol consumption; ultraviolet radiation (UVR) exposure; occupational carcinogens; high levels of radon; breastfeeding; hormone replacement therapy (HRT); human papilloma virus (HPV) and hepatitis B virus (HBV) vaccinations; bowel cancer screening; breast cancer screening; and cervical cancer screening.

3.1. Tobacco

Cigarette smoking is an established cause of cancer at multiple anatomic sites and is the single largest preventable cause of cancer in the EU. It is the main cause of lung cancer, responsible for eight in ten lung cancers. On average, approximately three in ten adults in the EU smoke. The risk of developing cancers of the lung, larynx, pharyngeal and oral cavity, oesophagus, stomach, pancreas, bladder and cervix decreases after quitting smoking (in comparison to those who continue smoking). Non-smoked forms of tobacco – varying in types and concentrations of carcinogens – are used in the EU by a much smaller proportion of the population than cigarettes. Smokeless tobacco users have excess risk of cancer of the oesophagus, pancreas and oral cavity; the magnitude of excess risk is depending on the content of carcinogens in smokeless tobacco, which for some products is low [16].

Second-hand smoke is an established cause of lung cancer and a possible cause of cancers of the larynx and pharynx [16]. In the EU, the domestic environment can be a place of frequent exposure of non-smokers to second-hand smoke. In addition, exposure to second-hand smoke still occurs to some degree in the work environment in several EU countries. Making the environment smoke-free, both at home and at work places, not only protects non-smokers from cancers caused by passive smoking but it also reduces the amount of smoking in active smokers [16].

Box 1. European Code Against Cancer.

EUROPEAN CODE AGAINST CANCER

12 ways to reduce your cancer risk

1. Do not smoke. Do not use any form of tobacco
2. Make your home smoke free. Support smoke-free policies in your workplace
3. Take action to be a healthy body weight
4. Be physically active in everyday life. Limit the time you spend sitting
5. Have a healthy diet:
 - Eat plenty of whole grains, pulses, vegetables and fruits
 - Limit high-calorie foods (foods high in sugar or fat) and avoid sugary drinks
 - Avoid processed meat; limit red meat and foods high in salt
6. If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention
7. Avoid too much sun, especially for children. Use sun protection. Do not use sunbeds
8. In the workplace, protect yourself against cancer-causing substances by following health and safety instructions
9. Find out if you are exposed to radiation from naturally high radon levels in your home; take action to reduce high radon levels
10. For women:
 - Breastfeeding reduces the mother's cancer risk. If you can, breastfeed your baby
 - Hormone replacement therapy (HRT) increases the risk of certain cancers. Limit use of HRT
11. Ensure your children take part in vaccination programmes for:
 - Hepatitis B (for newborns)
 - Human papillomavirus (HPV) (for girls)
12. Take part in organised cancer screening programmes for:
 - Bowel cancer (men and women)
 - Breast cancer (women)
 - Cervical cancer (women)

The European Code Against Cancer focuses on actions that individual citizens can take to help prevent cancer. Successful cancer prevention requires these individual actions to be supported by governmental policies and actions.

3.2. Diet, physical activity and healthy body weight

Imbalance between energy expenditure and energy intake promoted by an obesogenic environment leads to excess body fat, which increases risk of cancer at nine sites: oesophagus, colorectum, gall bladder, pancreas, breast (postmenopausal), endometrium, ovary, kidney, and prostate (advanced stage). Between 4% and 38% of these cancers – depending on site and sex – can be attributed to overweight/obesity [21].

Physical activity is a complex and multidimensional behaviour associated with decreased risks of colon, endometrial, and breast cancers, and less consistently with cancers of the lung, pancreas, ovary, prostate, kidney, and stomach. A substantial proportion of the European adult population currently fails to meet physical activity recommendations. Recently, sedentary behaviour, associated with cancer risk through weight gain, has also emerged as a potential independent determinant [22].

Diet influences the cancer process in several ways, both directly and indirectly, by affecting body fatness: high intakes of fruit and vegetables may reduce the risk of cancers of the aerodigestive tract, and dietary fibre protects against colorectal cancer; red and processed meats increase the risk of colorectal cancer; diets rich in high-calorie foods (such as fatty and sugary foods) promote excess energy intake and obesity, leading to increased risk of cancer [23].

3.3. Alcohol

Alcohol consumption is the third leading risk factor for disease and mortality in Europe and is a cause of cancers of the oral cavity,

pharynx, larynx, oesophagus, liver, colon, rectum and female breast, even for low and moderate alcohol intakes. It is estimated that 10% (confidence interval (CI): 7–13%) of all cancer cases in men and 3% (CI: 1–5%) of all cancer cases in women are attributable to alcohol consumption. The risk of cancer increases in a dose-dependent manner involving several biological mechanisms where ethanol and its genotoxic metabolite, acetaldehyde, play a major role [24].

3.4. Environment, occupation and radiation

UVR, another exposure modifiable by the individual, is the main cause of skin cancer (including cutaneous malignant melanoma, basal-cell carcinoma, and squamous-cell carcinoma), which is the most common cancer in fair-skinned populations. Excessive exposure from natural sources can be avoided by seeking shade, using appropriate clothing, and appropriately applying sunscreens. Exposure from artificial sources can be avoided by not using sunbeds or other tanning devices emitting UVR. Beneficial effects of sun or UV exposure, such as for vitamin D production, can be achieved while still avoiding too much sun exposure and avoiding the use of sunbeds [25].

People are exposed throughout life to a wide range of environmental and occupational pollutants from different sources at home, in the workplace, or in the general environment. Several chemicals, metals, dusts, fibres, and occupations have been established to be causally associated with an increased risk of cancers of the lung, skin and urinary bladder, and mesothelioma, among others. Regulations are not homogeneous across all countries in the EU, and protective measures in the workplace are not used consistently by all workers all of the time. Compliance with regulations needs to be continuously monitored. A recommendation to the individual is to follow safety instructions at the workplace [26].

Radon, a radioactive gas occurring naturally at high levels in some geographic locations, is a major source of exposure to ionising radiation. Indoor exposure to inhalation of radon and its decay products is an important cause of lung cancer, causing approximately one in ten lung cancers in Europe [6]. Exposures to radon in buildings can be reduced through a three-step process of identifying properties with potentially elevated radon levels, measuring radon levels, and reducing exposures by installation of remediation systems.

3.5. Breastfeeding

Breastfeeding is associated with a dose-dependent protective effect on breast cancer risk in both pre- and post-menopausal women, and a modest protective effect is suggested with regard to endometrial and ovarian cancers. Breast cancer is the most frequent cancer in women, showing rising incidence rates in EU countries over the past decades. Breastfeeding is also associated with a more rapid return to pre-pregnancy weight as well as a lower incidence of the metabolic syndrome, and it brings several health benefits to the child [27].

3.6. Hormone replacement therapy (HRT)

Consistent evidence exists that HRT, today almost solely prescribed as menopausal hormone therapy, is carcinogenic to humans and induces cancers in female genital organs and breast. The mechanisms underlying carcinogenicity include oestrogen-receptor-mediated responses and potentially direct genotoxicity of female hormones, hormone metabolites, or hormonal by-products – including reactive oxygen species [7]. Although HRT can only be obtained by prescription in most

Box 2. Guidance on the rationale behind the phrasing of each recommendation from the European Code against Cancer, 4th edition (given by item).

1. Do not smoke. Do not use any form of tobacco.

This specific item is intended to be a directive statement and to leave no room for interpretation.

2. Make your home smoke-free. Support smoke-free policies in your workplace.

The term 'home' covers a range of living environments. The word 'support' is positive, with connotations of being helpful and caring. This advice is intended to apply to smokers and non-smokers and recommends they uphold and defend the implementation of these policies.

3. Take action to be a healthy body weight.

This item recommends that people strive towards weight control. 'Take action' encompasses all actions that help a person work towards, or maintain, a healthy body weight. In this context, 'action' is not recommending specific activity, but leaving the specific actions to the reader.

4. Be physically active in everyday life. Limit the time you spend sitting.

'Physically active' is an inclusive term that encompasses all types of activity (not just specific forms of health-relevant activity such as gym use). The term 'everyday life' emphasises that this goes beyond allocating specific times to exercise and encourages active choices across all domains.

The second part of the recommendation focuses on sedentary time in the light of increasing evidence that it is a risk factor. We used the term 'sitting' because it is a more everyday term. We used 'limit' to imply that high rates of sitting should be avoided, without suggesting that sitting should be avoided completely.

5. Have a healthy diet:

- eat plenty of whole grains, pulses, vegetables and fruits;
- limit high-calorie foods (foods high in sugar or fat) and avoid sugary drinks;
- avoid processed meat, limit red meat and foods high in salt.

The word 'plenty' is used because it was considered a positive word with connotations of contentment.

The words 'avoid' and 'limit' are chosen because they seem to be a more 'gentle' form of advice, compared with 'do not eat' or 'cut out/down' – particularly as we are not expecting the public to entirely cut these foods out of their diet; this suggestion was seen as unrealistic in our public testing and was not well received due to the more authoritarian tone.

6. If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention.

This includes clarification that the recommendation applies to all types of alcohol, and uses the word 'if' so that the statement does not assume that all readers drink alcohol.

As discussed for recommendation #5, the word 'limit' is used first as this is a gentler way to advise about intake compared with directive alternatives such as 'drink less'.

The second statement raises awareness of the increased risk of cancer resulting from consumption of any amount of alcohol, consistent with current evidence, but not recommending total abstinence.

7. Avoid too much sun, especially for children. Use sun protection. Do not use sunbeds.

As before, 'avoid' is a softer way of advising that something should not be done than explicitly stating not to do it, and therefore has a less authoritarian tone.

The phrases concerning sun protection and sunbeds should be directive with no room for interpretation.

8. In the workplace, protect yourself against cancer-causing substances by following health and safety instructions.

The word 'protect' refers to keeping oneself safe and acknowledges that contact cannot be avoided completely.

The word 'following' is a softer and more positively perceived word for advising that something be done than alternatives such as 'abiding by' or 'adhering to'.

9. Find out if you are exposed to radiation from naturally high radon levels in your home. Take action to reduce high radon levels.

Inclusion of the phrase 'find out' prompts the reader's awareness that finding out is possible.

The word 'reduce' is a relative term used because the extent to which radon levels can be reduced may differ by property, area and personal capability. Absolute terms such as 'remove' would not be appropriate here.

'Home' is an inclusive term for all types of properties in which someone might live. House is not appropriate because it excludes some properties (e.g. flat, apartment, etc.).

10. For women:

- breastfeeding reduces the mother's cancer risk. If you can, breastfeed your baby;
- hormone replacement therapy (HRT) increases the risk of certain cancers; limit use of HRT.

'If you can' was included as it acknowledges some women cannot breastfeed. Without this phrase, we found that many readers in our test session took offence, regarding their choice of infant feeding method as their own affair.

'Limit' is a softer word for advising that HRT should only be used when necessary.

11. Ensure your children take part in vaccination programmes for:

- hepatitis B (for newborns);
- human papillomavirus (HPV) (for girls).

We are aware that vaccination policies vary across the EU and 'vaccination programme' was used to avoid giving a message that contradicts policies in place in some countries. 'Ensure' was chosen as a more positive way to recommend vaccination than 'vaccinate'.

12. Take part in organised cancer screening programmes for:

- bowel cancer (men and women);
- breast cancer (women);
- cervical cancer (women).

The word 'organised' clarifies that these are official regional or national programmes and not something the individual need necessarily seek out from commercial organisations. It also clarifies that we are not recommending screening over and above what is offered in each member country. Having one line per type of screening gives equal importance to each of them.

European countries, women should be informed about its risks in order to ensure an adequate basis for discussion with their physician on whether or not to use it.

3.7. Infections and vaccinations

Hepatitis B is a major cause of liver fibrosis, cirrhosis and cancer, all of which can be prevented with highly effective and safe vaccines that have been available for more than 30 years. Application of the vaccine to all newborns is the approach recommended by the World Health Organization (WHO) and the one applied in most countries in the EU. Several human papillomaviruses (HPVs) are causes of cancers of the cervix, vulva, vagina, anus, penis and oropharynx; highly effective and safe vaccines were licensed in 2006 and used in vaccination programmes in most European countries – aimed mainly at young adolescent girls. Other infections – such as hepatitis C, human immunodeficiency virus (HIV) and *Helicobacter pylori* – are recognised causes of cancer, and information is provided on level II of the Code [17].

3.8. Screening

For cancer screening the evidence demonstrates a benefit in terms of reduced specific mortality for colorectal, breast, and cervical cancers and of reduced incidence for cervical and colorectal cancers. The benefit substantially outweighs the potential harm of examining large numbers of people who may otherwise never have or suffer from these cancers. In the EU, bowel cancer is the third most common cancer and the second leading cause of death due to cancer, and breast cancer is the most common cancer and the most common cause of death due to cancer in women. Organised screening programmes are preferable because they provide better conditions to ensure that the EU quality assurance guidelines are followed in order to achieve the greatest benefit with the least harm. Screening programmes in the EU vary with respect to the age groups invited, the interval between invitations, and the different types of effective screening test used [18].

3.9. Role in cancer prevention

All the recommendations are considered to be important and associated with a relevant reduction in the cancer burden. The greatest benefit will come from adopting all recommendations. Although the associated cancer burden varies to some extent across the EU28, the recommendations are relevant to the EU28 as a whole. Therefore, there is no country-level weighting in the recommendations, although it was acknowledged that risk factors differ by (i) their relative risk for the individual, (ii) their dose–response shape, and (iii) their attributable fractions. Importantly, cigarette smoking remains the major single cause of cancer in Europe.

The footnote to the Code stating: “The European Code against Cancer focuses on actions that individual citizens can take to help prevent cancer. Successful cancer prevention requires these individual actions to be supported by governmental policies and actions” is an essential and important part of it (Box 1). It emphasises that most cancer risk factors have to be either complementarily or predominantly targeted at the population level with policies and regulations, the latter in particular with regard to exposure to environmental pollutants. There are numerous carcinogenic chemicals in our environment, for which appropriate regulation leads to a reduction in the cancer burden, and many are indeed regulated in the EU [28]. A recent prominent example is air pollution, classified as a human carcinogen in 2013 [29], and estimated to account for just over 7% of lung cancers for ambient air and just over 1% for household air pollution from solid fuels in the EU [26], despite regulation being in place.

3.10. Communication of the recommendations

From a communication point of view the following were important to have: a limited number of items, brevity and simplicity of each message, consistent tone, everyday language, gentle directive tone (advisory rather than merely informative), and avoidance of fear creation. Some explanations of the wording and phrases are given in Box 2 for each recommendation.

4. Discussion

4.1. Reducing the cancer burden in Europe

With EU28's 504.6 million inhabitants in 2012, the estimated 2.64 million new cancer cases and 1.28 million cancer deaths (not

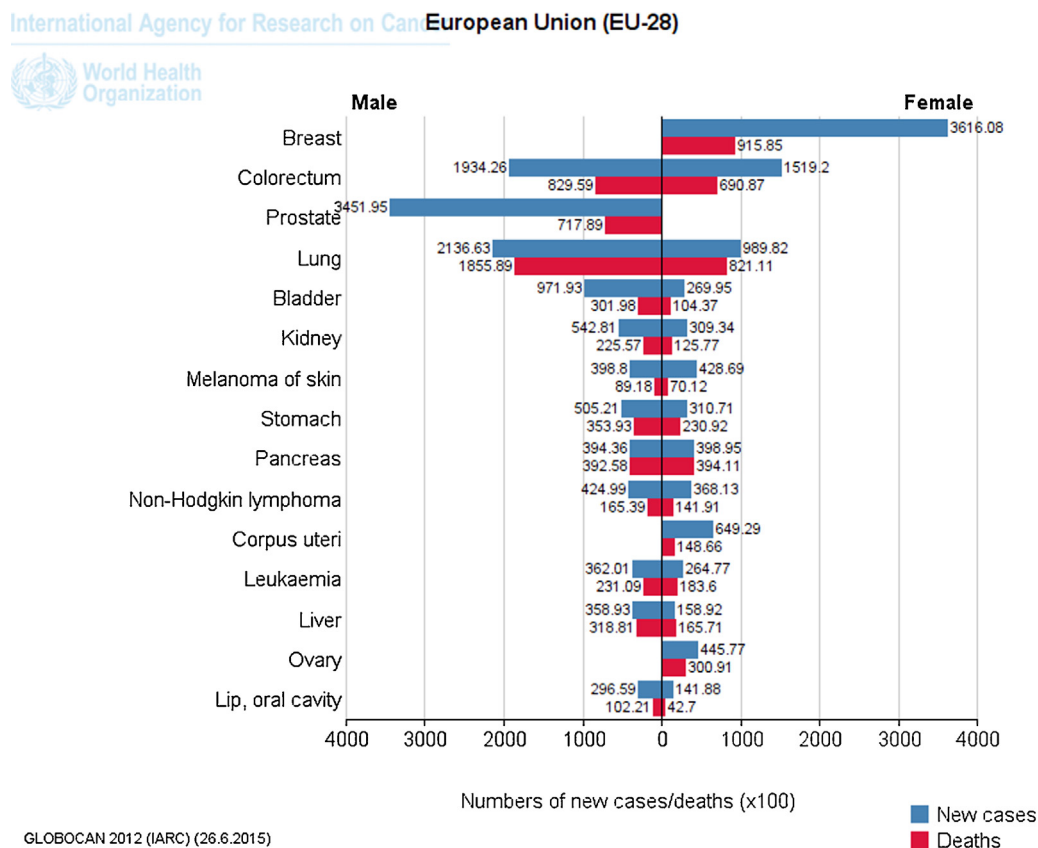
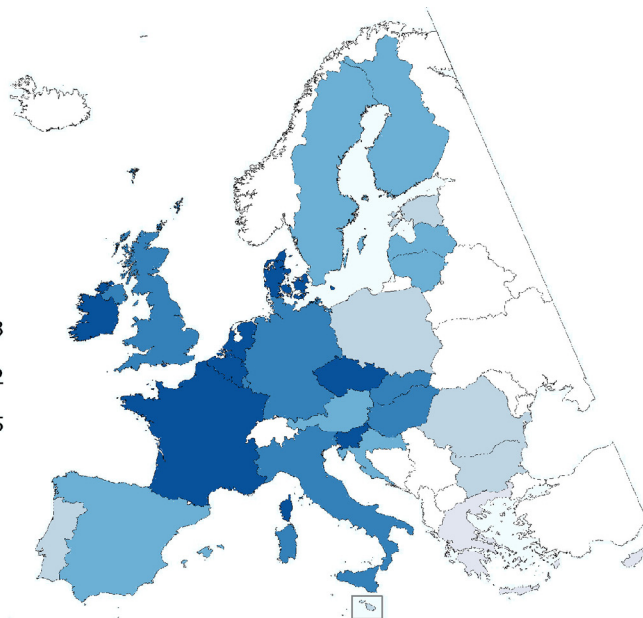
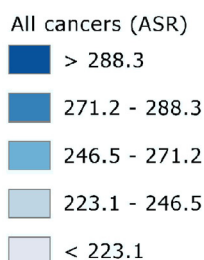


Fig. 3. Number of new cancer cases and cancer deaths for the top 15 commonest cancers in the 28 member states of the European Union; estimate for 2012 by IARC GLOBOCAN.

counting non-melanoma skin cancer) represent a major disease burden in the European population [1]. The most common cancer in EU28 was cancer of the female breast with 362,000 new cases in 2012, followed closely by prostate cancer with 345,000 new cases (Fig. 3). Other cancers in the top 15 shown in Fig. 3 are colorectal cancer, lung cancer, bladder cancer, kidney cancer, skin melanoma, stomach cancer, pancreatic cancer, non-Hodgkin lymphoma, cancer of the uterus, leukaemia, liver cancer, ovarian cancer, and cancer of lip and oral cavity. When looking at cancer deaths, lung cancer remains the largest contributor to the overall burden, with a total of 268,000 deaths in 2012 in men and women combined. This is particularly striking from a prevention point of view, as the main risk factors for lung cancer have been characterised; most lung cancers are indeed preventable, tobacco smoking accounting for

the by far largest proportion of lung cancers, with contributions from other environmental factors (e.g. air pollution, radon) and occupational exposures (such as asbestos) [4]. Colorectal cancers accounted for 152,000 cancer deaths in EU28, followed by female breast cancer and prostate cancer (Fig. 3). The poorest survival among the top 15 cancers was seen for pancreatic cancer, resulting in a total number of deaths almost as high as the number of new cases (Fig. 3). Cancer rates differ across Europe; Fig. 4 shows the age-standardised incidence and mortality rates for all cancers combined (and both genders combined) for the EU28 countries, estimated for 2012. There is some variation across the EU28, with higher overall cancer incidence rates in some Northern and Western European countries, while cancer mortality is highest in Eastern Europe.

Incidence



Mortality

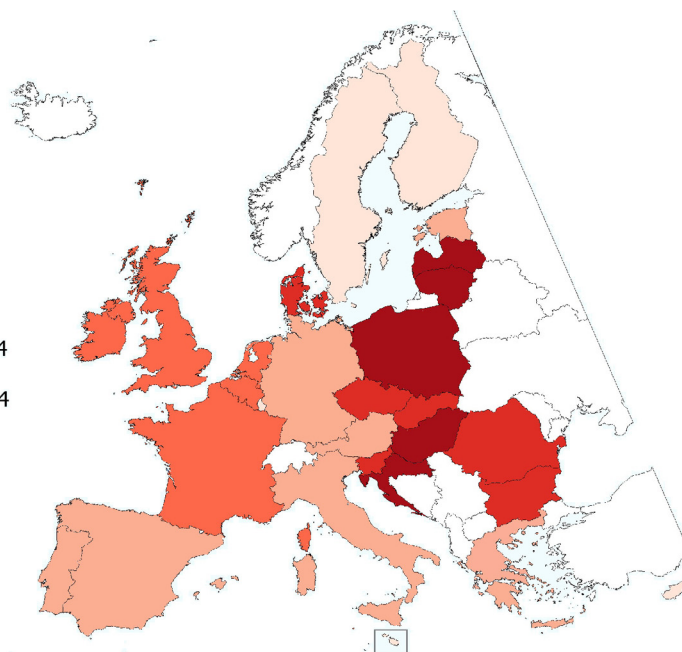
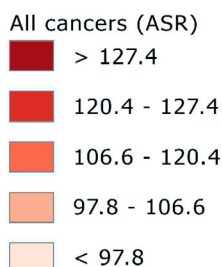


Fig. 4. Incidence and mortality of all cancers combined (excluding non-melanoma skin cancer) in the 28 EU countries, men and women combined; shown as age-standardised rates (ASRs) per 100,000. Source: GLOBOCAN 2012.

As discussed above, it has been estimated that up to half of the cancer burden is preventable, with successful prevention being a combination of individual preventive action (by avoiding or reducing harmful exposures) and group action (when exposure is eliminated or reduced by measures effective at the population level) [3,4]. The first type usually aims to modify individual behaviours: for instance quitting smoking or maintaining a healthy body weight. The second type usually relates to regulatory frameworks, for instance establishing smoke-free environments, implementing worker protection, urban design conducive to active living, or developing safety standards to protect citizens from harmful exposure to pollutants in the general environment or the workplace. Individual and group measures may be complementary and inter-dependent, for example by informing individuals how to quit smoking within a supportive regulatory framework: including tax and price policies, making access to tobacco more difficult, or legally enforcing smoke-free environments [30–32]. Vaccination or screening programmes have to be set up by health authorities, but individuals have to actively participate. Some exposures, however, are difficult to avoid by the individual alone and then regulatory action has an essential role; an example is air pollution. Nevertheless, each individual can contribute to overall better air quality by, for example, avoiding unnecessary car use, thereby contributing to a healthier environment leading to fewer cancers on a population level.

Vaccines prevent cancer by avoiding chronic infection with carcinogenic viruses [33,34]. Screening prevents cancer by detection of curable pre-cancerous lesions, and reduces cancer mortality by early detection of asymptomatic cancers in more curable stages [35]. Vaccines and screening may target the same cancer, as for example cancer of the uterine cervix. Early detection is advisable only when it is scientifically established that the benefits of mortality reduction of a specific cancer outweigh possible harms: for example those of over-diagnosis and related treatment [35]. The scientific evidence of efficacy of screening for a specific cancer (reduction of mortality for curable cancers and of incidence for preventable cancers) is a necessary but insufficient condition for screening implementation; a favourable balance between screening benefits and harms should exist.

The European Code against Cancer is a key prevention tool, providing information to the individual on how to reduce their risk of cancer. The Code should also form a base to guide national health policies in cancer prevention, as well as calls for complementary measures on a society level to protect the population and to assist the individual in reducing their cancer risk.

4.2. Conclusions on the 4th edition of the European Code against Cancer

The 4th edition of the European Code against Cancer was developed using a rigorous scientific process. The process was based on: (i) identification of causes of cancer and preventive interventions using recent comprehensive authoritative sources of scientific evidence; (ii) evaluation of the science by experts supported by new systematic literature searches (reviews) where necessary; (iii) advice on effective communication to the general population; (iv) oversight by a pan-European Scientific Committee of senior experts of leading European institutions of cancer research and prevention.

The outcome comprises three levels of information (Fig. 1) that are contained in an *ad-hoc* website [25]: (i) the European Code against Cancer itself comprising “12 ways to reduce your cancer risk”; (ii) additional information, in the form of questions and answers, on risk factors, and what individuals can do protect themselves; (iii) the scientific justification of the recommendations published in the peer-reviewed literature.

The European Code against Cancer has the potential to be scaled up to the global level, and to be broken down by regions of the world, using the scientific methodology that was established and with similar presentation of outcomes.

Conflicts of interest

Dr. Puska reports to have begun serving as chair of the International Advisory Board of MEDIETA Ltd., a commercial entity that manufactures mobile patient monitoring systems, in June 2014 after completion of work on the development of the European Code against Cancer. Dr. Wiestler reports having served as chair of the Scientific Advisory Boards for Siemens and Bayer. Dr. Cavalli reports having been involved in an international Phase III trial (iELSG Trial 19) from Roche.

The other authors declare no conflict of interest.

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Appendix

The ‘Working Group of Scientific Experts’ consists of the following authors:

(Tobacco): Neela Guha, Eva Kralikova, Anne McNeill, Armando Peruga; (Nutrition): Annie Anderson, Franco Berrino, Marie-Christine Boutron-Ruault, Michele Cecchini, Tim J. Key, Michael Leitzmann, Teresa Norat, Hilary J. Powers, Chiara Scoccianti; (Radiation): Anssi Auvinen, Esther de Vries, Friederike Erdmann, Rüdiger Greinert, John Harrison, Ausrele Kesminiene, Neil McColl; (Environment and occupation): Søren Friis, Manolis Kogevinas, Rodolfo Saracci, Kurt Straif, Harri Vainio; (Infections): Maribel Almonte, Ahti Anttila, Hugo De Vuyst, Joakim Dillner, Silvia Franceschi, Paula Gonzalez, Andrew Hall, Jin Young Park; (Screening): Paola Armaroli, Wendy Atkin, Peter B. Dean, Harry de Koning, Lena Dillner, Ernst Kuipers, Iris Lansdorp-Vogelaar, Eugenio Paci, Jaroslaw Regula, Eero Suonio, Sven Törnberg; (Communication): Lynn Faulds Wood, Nicolas Gaudin, Kirstin Grosse Frie, Veronique Terrasse, Kelly Winstanley; (Literature): Cristina Bellisario, Elena Biagioli, Michela Cinquini, Silvia Gianola, Marien Gonzalez Lorenzo; (Secretariat): Lawrence von Karsa, Tracy Lignini; experts listed by working group only if not co-authors and only by first appearance.

References

- [1] Eurostat news release 25 November 2014; <http://ec.europa.eu/eurostat/documents/2995521/6131615/3-25112014-BP-EN/aab2c2d3-aed9-430a-a561-e188b8ef49d8>.
- [2] Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin D, Forman D, Bray F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 11. Lyon, France: International Agency for Research on Cancer, 2013.
- [3] Parkin DM, Boyd L, Walker LC. The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010. *Br. J. Cancer* 2011;105(Suppl): S77–81.
- [4] Danaei G, Vander Hoorn S, Lopez AD, Murray CJ, Ezzati M, Comparative Risk Assessment collaborating group (Cancers). Causes of cancer in the world:

- comparative risk assessment of nine behavioural and environmental risk factors. *Lancet* 2005;366(9499):1784–93.
- [5] Boyle P, Autier P, Bartelink H, Baselga J, Boffetta P, Burn J, et al. European Code Against Cancer and scientific justification: third version (2003). *Ann. Oncol.* 2003;14(7):973–1005.
 - [6] McColl N, Auvinen A, Kesminiene A, Espina C, Erdmann F, de Vries E, et al. European Code against Cancer 4th Edition: ionising and non-ionising radiation and cancer. *Cancer Epidemiol* 2015;39:S93–100.
 - [7] Friis S, Kesminiene A, Espina C, Auvinen A, Straif K, Schüz J. European Code against Cancer 4th Edition: medical exposures, including hormone therapy, and cancer. *Cancer Epidemiol* 2015;39:S107–19.
 - [8] Minozzi S, Armaroli P, Espina C, Villain P, Wiseman M, Schüz J, et al. European Code against Cancer 4th Edition: process of reviewing the scientific evidence and revising the recommendations. *Cancer Epidemiol* 2015;39:S11–9.
 - [9] International Agency for Research on Cancer. Agents Classified by the IARC Monographs, Volumes 1–109. International Agency for Research on Cancer; 2013. <http://monographs.iarc.fr/ENG/Classification/index.php>.
 - [10] Coglian VJ, Baan R, Straif K, Grosse Y, Lauby-Secretan B, El Ghissassi F, et al. Preventable exposures associated with human cancers. *J. Natl. Cancer Inst.* 2011;103(24):1827–39.
 - [11] World Cancer Research Fund/American Institute for Cancer Research. Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective. Washington, DC: AICR, 2007.
 - [12] World Cancer Research Fund/American Institute for Cancer Research. Continuous Update Project Findings & Reports; 2015. <http://www.wcrf.org/int/research-we-fund/continuous-update-project-findings-reports>. (accessed 17.02.15).
 - [13] Greenhalgh T. Why read paper at all? In: How to Read a Paper: The Basics of Evidence-Based Medicine. BMJ Books; 1997. 1–14.
 - [14] O'Connor D, Green S, Higgins JPT. Defining the review question and developing criteria for including studies. In: Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions* (Wiley Cochrane Series) (Hardcover). UK: Wiley-Blackwell, 2008.
 - [15] Richardson WS, Wilson MC, Nishikawa J, Hayward RS. The well-built clinical question: A key to evidence-based decisions. *ACP J. Club* 1995;123(3):A12–3.
 - [16] Leon ME, Peruga A, McNeill A, Kralikova E, Guha N, Minozzi S, et al. European Code against Cancer, 4th Edition: tobacco and cancer. *Cancer Epidemiol* 2015;39:S20–33.
 - [17] Villain P, Gonzalez P, Almonte M, Franceschi S, Dillner J, Anttila A, et al. European Code against Cancer 4th Edition: infections and Cancer. *Cancer Epidemiol* 2015;39:S120–38.
 - [18] Armaroli P, Villain P, Suonio E, Almonte M, Anttila A, Atkin WS, et al. European Code against Cancer, 4th Edition: cancer screening. *Cancer Epidemiology* 2015;39:S139–52.
 - [19] European Commission. Health and Food Safety; 2015. http://ec.europa.eu/dgs/health_consumer/dyna/enews/enews.cfm?al_id=1537. (accessed 17.02.15).
 - [20] International Agency for Research on Cancer. European Code Against Cancer; 2015. <http://cancer-code-europe.iarc.fr/index.php/en/>. (accessed 17.02.15).
 - [21] Anderson AS, Key TJ, Norat T, Scoccianti C, Cecchini M, Berrino F, et al. European Code against Cancer 4th Edition: obesity, body fatness and cancer. *Cancer Epidemiology* 2015;39:S34–45.
 - [22] Leitzmann M, Powers H, Anderson AS, Scoccianti C, Berrino F, Boutron-Ruault M-C, et al. European Code against Cancer 4th Edition: physical activity and cancer. *Cancer Epidemiol* 2015;39:S46–55.
 - [23] Norat T, Scoccianti C, Boutron-Ruault M-C, Anderson A, Berrino F, Cecchini M, et al. European Code against Cancer 4th Edition: diet and cancer. *Cancer Epidemiology* 2015;39:S56–66.
 - [24] Scoccianti C, Cecchini M, Anderson AS, Berrino F, Boutron-Ruault M-C, Espina C, et al. European Code against Cancer 4th Edition: alcohol drinking and cancer. *Cancer Epidemiology* 2015;39:S67–74.
 - [25] Greinert R, de Vries E, Erdmann F, Espina C, Auvinen A, Kesminiene A, et al. European Code against Cancer 4th Edition: ultraviolet radiation and cancer. *Cancer Epidemiol* 2015;39:S75–83.
 - [26] Espina C, Straif K, Friis S, Kogevinas M, Saracci R, Vainio H, et al. European Code against Cancer 4th Edition: environment, occupation and cancer. *Cancer Epidemiol* 2015;39:S84–92.
 - [27] Scoccianti C, Cecchini M, Anderson AS, Berrino F, Boutron-Ruault M-C, Espina C, et al. European Code against Cancer 4th Edition: alcohol drinking and cancer. *Cancer Epidemiology* 2015;39:S67–74.
 - [28] Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency. L 396, 30.12.2006, 1–849., European Union, (2006).
 - [29] Loomis D, Grosse Y, Lauby-Secretan B, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, et al. The carcinogenicity of outdoor air pollution. *Lancet Oncol.* 2013;14(13):1262–3.
 - [30] Wilson LM, Avila Tang E, Chander G, Hutton HE, Odelola OA, Elf JL, Heckman-Stoddard BM, Bass EB, Little EA, Haberl EB, Appelberg BJ. Impact of tobacco control interventions on smoking initiation, cessation, and prevalence: a systematic review. *J. Environ. Public Health* 2012;2012:961724.
 - [31] Fichtenberg CM, Glantz SA. Effect of smoke-free workplaces on smoking behaviour: systematic review. *BMJ* 2002;325(7357):188.
 - [32] Sussman S, Levy D, Lich KH, Cené CW, Kim MM, Rohrbach LA, Chaloupka FJ. Comparing effects of tobacco use prevention modalities: need for complex system models. *Tob. Induc. Dis.* 2013;11(1):2. <http://dx.doi.org/10.1186/1617-9625-11-2>.
 - [33] Sun Z, Chen T, Thorgeirsson SS, Zhan Q, Chen J, Park JH, et al. Dramatic reduction of liver cancer incidence in young adults: 28 year follow-up of etiological interventions in an endemic area of China. *Carcinogenesis* 2013;34(8):1800–5.
 - [34] Schiller JT, Castellsagué X, Garland SM. A review of clinical trials of human papillomavirus prophylactic vaccines. *Vaccine* 2012;30(Suppl 5):F123–38.
 - [35] von Karsa L, Dean PB, Arrossi S. Opportunities and constraints for cancer screening. In: Wild C, Stewart B, eds. *World Cancer Report 2014*. Lyon: International Agency for Research on Cancer; 2014.